

Claims

1. A method for screening of cellular responses comprising:

(a) providing a solid porous support having first and second surfaces and at least one area with a plurality of through-going channels;

(b) providing cellular components on said first and/or second surface of said solid porous support, wherein said solid porous support retains said cellular compounds on its surface;

(c) providing a supply chamber at said first and/or second surface and opposite to said cellular components;

(d) subjecting all or part of said cellular components to one or more effectors; wherein at least one effector is delivered from said supply chamber through the porous support;

(e) incubating the said all or part of cellular components with said effectors under conditions allowing the induction of cellular responses in the said all or part of cellular components;

(f) optionally providing detector molecules to the said all or part of cellular components for assaying cellular responses

(g) assaying for cellular responses; and,

(h) identifying and characterizing the cellular responses induced by said effector molecules.

2. The method according to claim 1 wherein said supply chamber comprises at least 1 compartment.

3. The method according to claim 2, wherein said at least one compartment is provided with a liquid medium comprising at least one effector molecule.

4. The method according to claims 2 or 3, wherein said at least one compartment is provided with a liquid medium comprising a gradient of at least one effector molecule.

5. The method according to claims 2 to 4, wherein said at least one compartment is provided with a liquid medium comprising a 2D gradient of at least two effector molecules.

6. The method according to any of claims 1 to 5, wherein said effector molecules are chosen from the group comprising nutrients, enzyme substrates, test compounds, inducer molecules, chaperone proteins, hormones, oligopeptides, nucleic acids, agonists, antagonists, inhibitors of cellular functions, enhancers of cellular functions,
5 transcription factors, growth factors, differentiation-inducing agents, secondary metabolites, toxins, glycolipids, carbohydrates, antibiotics, mutagens, drugs, proteins, antibodies, antibody fragments, modified analogues thereof, and any combination thereof.
- 10 7. The method according to any of claims 1 to 6, wherein said supply chamber is in liquid contact with said first and/or said second surface of said solid support.
8. The method according to any of claims 1 to 7, wherein the said at least one effector molecule is transported passively or actively through said porous support.
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9. The method according to any of claims 1 to 8, wherein the said at least one effector molecule diffuses through said porous support to the cellular components by contact force.
- 20 10. The method according to any of claims 1 to 8, wherein the said at least one effector molecule is transported actively through said porous support by pumping, magnetically, electrically, or by piezo-electronic force.
- 25 11. The method according to any of claims 1 to 10, wherein said providing of cellular components on the surface of a support is by a deposit directly on said support of an inoculum, culture, solution, or mixtures thereof.
- 30 12. The method according to any of claims 1 to 11, wherein said cellular components are selected from the group comprising mammalian cells, insect cells, yeast cells, fungal cells, plant cells microbial cells, bacterial cells, cellular vesicles, cellular organelles, tissue sections, whole organisms including nematodes.
- 35 13. The method according to any of claims 1 to 12, wherein said detector molecules are selected from the group comprising nucleic acids including modified analogues thereof; peptides and oligopeptides including modified analogues thereof; proteins;

antibodies including antibody fragments; aptamers; enzyme substrates; carbohydrates; specific dyes; and combinations thereof.

14. The method according to any of claims 1 to 13, wherein said cellular responses are
5 chosen from the group comprising chemically induced or physiological events in the
cell including lysis; apoptosis; growth inhibition; growth promotion; morphology
changes; cell differentiation; organelle movement; changes in metabolite
concentrations or metabolite patterns; changes in cellular contents including changes
10 in mRNA level, protein composition, lipid composition, carbohydrate composition,
production of a protein, secretion of a protein, surface exposure of a protein, or other
molecule of interest by the cell; membrane surface molecule activation including
receptor activation; trans-membrane ion transports; stage of infection to viruses,
prions or cellular pathogens or resistance to such pathogens; and cell-cell interactions
15 including changes to communities or mixtures of cells.

15. The method according to claim 14, wherein said molecule of interest is selected from
the group comprising peptides, oligopeptides, lipopeptides, glycosylated peptides,
antimicrobial peptides, polypeptides, proteins, enzymes, antimicrobial molecules,
primary and secondary metabolites, and small organic molecules including
20 pharmaceutical molecules and pharmacophores.

16. The method according to any of claims 6 to 15, wherein said effector is a drug or any
compound which is useful in the discovery process of a drug candidate.

17. The method according to claim 16, wherein said effector is a drug selected from a
chemical or natural drug candidate library.

18. The method according to any of claims 1 to 17, wherein said cellular response is
assayed in whole broth or cell culture medium, in isolated cells such as pelleted cells,
30 in supernatant of the cellular components, or in lysate of the cellular components.

19. The method according to any of claims 1 to 18, wherein said assaying of cellular
responses is by: detecting the presence or absence of a change in detectable signal,
the presence of a change in detectable signal indicating a cellular response.

20. The method according to any of claims 1 to 19, wherein delivery of at least one effector is from above the support by a means chosen from the group comprising a delivery mask, a microfluidics device, a high precision x-y-z micro-pipettor, inkjet printer, and manual handling.

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21. The method according to any of claims 1 to 20, wherein said identifying of the cellular responses is by a method chosen from the group comprising luminescence, regular light microscopy, and electron microscopy.

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22. The method according to claim 21, wherein said luminescence is fluorescence or phosphorescence.

23. The method according to any of claims 1 to 22, wherein said solid support is a flow-through solid support.

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24. The method according to any of claims 1 to 23, wherein said solid support is a metal oxide solid support.

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25. The method according to claim 24, wherein said metal oxide solid support is an aluminium oxide solid support.

26. The method according to any of claims 1 to 25, wherein said assaying is performed in real-time.

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27. The method according to any of claims 1 to 25, wherein said assaying is an end-point assaying.

28. The method according to any of claims 1 to 27, wherein said cellular components are pre-labelled by introduction of a luminescent indicator.

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29. The method according to any of claims 1 to 28, wherein said detector molecules are present within the pores of the solid support prior to providing cellular components and effectors.

30. Use of a method according to any of claims 1 to 29, for monitoring induced cellular responses of host cells.
- 5 31. Use of a method according to any of claims 1 to 29, for monitoring real-time growth kinetics on-chip.
32. Use of a method according to any of claims 1 to 29, for monitoring cell morphology.
- 10 33. Use of a method according to any of claims 1 to 29, for monitoring cell behaviour.
34. Use of a method according to any of claims 1 to 29, for monitoring sub-cellular vesicle trafficking.
- 15 35. Use of a method according to any of claims 1 to 29, for on-chip recombination, transformation or viral introduction of cellular components.
36. Use of a method according to any of claims 1 to 29, for functional screening of cellular responses upon assaying host cells or organisms with test compounds.
- 20 37. Use of a method according to any of claims 1 to 29, for biofilm modelling.
- 25 38. A device for performing a method according to any of claims 1 to 28, comprising a solid porous support; said support being at its first and/or second surface in liquid contact with a supply chamber or in gaseous contact or wherein said supply chamber may be physically attached thereto; wherein said supply chamber comprises multiple-use insertions, said multiple-use insertions are fixed or movable separations and wherein the spatial organization of the inserts determines the number of compartments.
- 30 39. The device according to claim 38, wherein said supply chamber comprises at least one compartment.
- 35 40. The device according to claims 38 or 39, wherein an array of test compounds is provided within predefined regions on the surface of said support, said test compounds are in solid, liquid, gaseous or supercritical state.

41. The device according to any of claims 38 to 40, wherein an array of cellular components is provided in predefined regions on the surface of said support.

5 42. The device according to claim 41, wherein said cellular components are conditioned for preservation on said support.

43. The device according any of claims 38 to 40, wherein a cellular component is provided on the surface of said support.

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44. The device according to claim 43, wherein a cellular component is provided on the surface of said support, said cellular component being conditioned for preservation on said support.

15 45. The device according to any of claims 38 to 44, wherein an array of detector molecules is immobilized within said porous support.

46. The device according to claim 45, wherein said array of detector molecules comprises a plurality of equal detector molecules or a plurality of different detector molecules.

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47. The device according to claim 42 or 44, wherein said condition is chosen from the group comprising lyophilization, liquid nitrogen and glycerol dissolution.

25 48. A solid porous support, wherein within its porous structure an array of chemical compounds is provided in dried, lyophilized, gaseous or supercritical state

49. A supply chamber for spatial delivery of one or more effectors through a porous solid support comprising:

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(a) multiple-use insertions, said multiple-use-insertions are fixed or movable separations and wherein the spatial organization of the inserts determines the number of compartments, said supply chamber comprising at least one compartment, said at least one compartment allowing said delivery of one or more effectors through part or all of the channels within said porous solid support;

(b) means for compartment alignment towards predefined regions on the support;

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(c) means of adding or removing or changing the amounts of effectors.

50. The supply chamber according to claim 49, wherein said at least one compartment is provided with one or more effectors for performing a method according to any of claims 1 to 29.

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51. The supply chamber according to claim 50, wherein said at least one or more effectors is contained within a gaseous or liquid medium.

52. Use of a device according to any of claims 38 to 47, for cell-based assays according to a method as described in any of claims 1 to 28.

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53. Use of a device according to any of claims 38 to 47 for applications as defined in any of claims 30 to 37.

54. A kit for performing a method according to any of claims 1 to 29, comprising a device according to any of claims 38 to 47.

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